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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,512	08/26/2003	Friedhelm Hildebrandt	UM-08333	5258

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EXAMINER	
GRUN, JAMES LESLIE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/648,512	HILDEBRANDT ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 Aug 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Invention I, claims 1-8 and 21-22 in the paper filed 27 July 2006 is acknowledged. Claims 9-20 have been cancelled.

The disclosure is objected to because of the following informalities: page 13, lines 10 and 16, it is believed --least-- was intended. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-8, 21, and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant desires an assay for the detection of nephronophthsis type 4 by detection of a variant polypeptide in patient samples from that encoded by the *NPHP4* genomic sequence in normals. However, the predictable presence of the intact polypeptide in any sample is not

described or supported by the specification, particularly for the suggested samples of blood, urine, or amniotic fluid. The specification teaches that the encoded protein has no signal sequence and no transmembrane regions, yet contains a putative nuclear localization signal (see page 104). Thus, given the unknown ability of the unknown cells which may express the polypeptide to even release the polypeptide, the presence of sufficient quantities of this putative nuclear protein in a body fluid sample for detection are entirely unknown, unpredictable, and suspect to one in the art. Moreover, even if assuming that the polypeptide is released from damaged cells, again there is no predictability for its detection and, moreover, endogenous enzymes may cleave the protein in unknown and unpredictable ways such that the ability to discriminatingly detect a truncated version from an intact polypeptide in patients versus normals is also unknown, unpredictable, and questionable to one in the art. Applicant fails to specifically identify, and fails to provide antibodies specific for, any epitope of the polypeptide, or any other means, which predictably can be used to discriminatingly detect a truncated version in any samples from patients versus normals. Moreover, applicant does not describe nor provide guidance for the performance of a gel free truncation test with a sample comprising polypeptide. The test as described (page 63) requires translation of nucleic acid. Absent further written description and guidance from applicant, one would have no assurance of the ability to identify relevant samples, to identify, make and use relevant reagents, and to predictably perform the invention as instantly claimed. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for

vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Since the claimed invention is not enabled, as set forth above, the instant application is not entitled to a claim of priority to any earlier filed applications. Thus, for the purposes of art rejections, the date accorded the subject matter of the instant application (until such time as enablement may be established) is the filing date of the application, 26 August 2003.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 21, and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, "the" presence or absence lack antecedent basis. In claims other than those dependent upon claim 2, it is not clear what is encompassed by a nephroretinin polypeptide or a variant thereof because it is not clear how one performs the

correlation with nephronophthisis (see page 12) to determine what structures are within the metes and bounds of the invention.

In claims 8 and 21, the property of "differential antibody binding" is not clear because it is not clear what binding is compared to determine a difference and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In claim 21, it is not clear how binding to two epitopes indicates a differential.

In claim 21, "the" C-terminus or N-terminus lack antecedent basis and are not clear as to what the antibodies are binding.

In claim 22, the relationships of the components of the method are not clear because the use of a gel free truncation test to detect polypeptide in a sample is not clear.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1 and 4-8 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Mollet et al. (Nature Genet. 32: 300, Oct. 2000).

Mollet et al. detected a variant of instant SEQ ID NO: 2 in human embryonic kidney cell lysate samples with an antibody. The detected polypeptide comprised a N-terminal truncation of the sequence as instantly disclosed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ishikawa et al. (DNA Res. 5: 169, 1998) disclose the sequence of the cDNA clone KIAA0673 encoding a large protein, which, in light of the instant disclosure and that of Mollet et al. is at least a variant of nephroretinin/nephrocystin-4.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JLG

James L. Grun, Ph.D.
October 18, 2006

LONG V. LE 10/21/06
SUPERVISORY PATENT EXAMINER
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